

IN THE SPECIFICATION

Please amend pages 1,2, 3, 5, 7, 12 and 18 as follows:

On page 1, please replace paragraph 1, lines 5-10 with the following amended paragraph:

1. Field of the Invention

The present invention application is a divisional application of US patent application Serial No. 09/270,465, now US Patent No. 6,313,267, which application is a continuation of 08/568,310, now US Patent No. 5,976,832 and relates to novel calcium-binding proteins, DNA encoding them, antibodies against the calcium-binding proteins, hybridomas producing the antibodies, diagnostic agents comprising the antibodies, etc.

On page 2, please replace paragraph 5, lines 32-35, with the following amended paragraph:

Thus, the present invention provides calcium-binding proteins which may comprise any amino acid sequence which is substantially identical to the amino acid sequence encoded by nucleotide sequence shown in SEQ ID NO: 1 or 12.

On page 3, please replace paragraph 4, lines 15-22, with the following amended paragraph:

Fig. 1 shows the amino acid sequence of bovine calcium-binding protein and the DNA sequence encoding it (SEQ ID NO. 1). In Fig. 1, the lines labeled as N indicate the results of determining the N-terminal amino acid sequence of the protein, and the dotted lines labeled as V8-P indicate the amino acid sequence of the two peptide fragments produced when the protein was cut with *S. aureus* V8 proteinase.

On page 3, please replace paragraph 5, lines 32, with the following amended paragraph:

Fig. 2 shows the amino acid sequence of bovine calcium-binding protein and the DNA sequence encoding it (SEQ ID NO: 2). In Fig. 2, the lines labeled as N indicate the results of determining the N-terminal amino acid sequence of the protein, the dotted lines labeled as V8-P indicate the amino acid sequence of the two peptide fragments produced when the protein was cut with *S. aureus* V8 proteinase, and broken lines labeled as Lysyl-P indicate the amino acid sequence of fragments produced when the protein was cut with lysylendopeptidase.

On page 3, please replace paragraph 6, lines 33-36, with the following amended paragraph:

Fig. 3 3A shows electrophoretic patterns of bovine amniotic fluid with a Tricine-SDS-PAGE silver staining gel (A) and

Fig. 3B shows the $^{45}\text{Ca}^{2+}$ overlay autoradiogram after Tricine-SDS-PAGE (B).
~~In~~ In Fig. 3A and Fig. 3B, lane 1 represents.

On page 5, please replace paragraphs 2 and 3, with the following amended paragraphs:

The calcium-binding protein of the present invention comprises any amino acid sequence ~~which is substantially identical to the amino acid sequence which is~~ substantially identical to the amino acid sequence encoded by the nucleotide sequence listed in SEQ ID NO: 1 or 12. By "substantially identical" is meant that it is either exactly identical or is modified at one or a few amino acids while retaining the calcium-binding activity. "Modified" as used here refers to a change in the amino acid sequence encoded by the nucleotide sequence listed in SEQ ID NO: 1 or 12 by a deletion, addition or amino acid substitution, or a combination thereof.

Furthermore, "a few" means less than, for example, about 10% of the entire number of amino acids of the amino acid sequence listed in SEQ ID NO: ~~4 or 12~~ 19 or 20, such as 10 or fewer, and preferable 5 or fewer. Thus, according to the present invention, any amino acid sequence which is substantially identical to the amino acid sequence listed in SEQ ID NO: ~~4 or 12~~ 19 or 20 encompasses amino acid sequences with an addition, deletion or substitution of 1 to 10, and preferably 1 to 5 amino acids which still have calcium-binding activity.

Page 7, please replace paragraph 2, with the following amended paragraph:

The calcium-binding protein having the amino acid sequence encoded by the nucleotide sequence listed as Sequence No. 1 or 12 may be isolated or purified from, for example, bovine amniotic fluid or other tissue, or human tissues. The isolation or purification may be performed by combining any of a variety of known purification methods, to the required degree of purity. Methods of purification which may be used include cationic exchange, anionic exchange, gel filtration, hydrophobic, isoelectric, immunologic affinity, chelate affinity, reverse phase and other kinds of chromatography, as well as fractional precipitation, etc. Other methods may also be used.

Page 11, please replace paragraph 2, with the following amended paragraph:

The present invention provides a gene, typically DNA, encoding the protein of the present invention, for production of the protein. This DNA typically has the nucleotide sequence listed in SEQ ID NO: 1 or 12, but it is not limited thereto, and DNA having various nucleotide sequences with degeneration of the codons coding for the amino acid sequence listed in SEQ ID NO: 1 or 12 are also included in the present invention. Furthermore, the above description implies that DNA encoding proteins which comprise amino acid sequences which are substantially identical to the amino acid sequence encoded by the nucleotide sequence listed in SEQ ID NO: 1 or 12 are also included in

the present invention. DNA encoding protein fragments or fused proteins of the above-mentioned protein is also included in the present invention.

Page 12, please replace paragraph 4, with the following amended paragraph:

DNA encoding amino acid sequences which are not identical to but are substantially identical to the amino acid sequence encoded by the nucleotide sequence listed in SEQ ID NO: 1 or 12, such as amino acid sequences modified by one or a few amino acid additions, deletions or substitutions, may be prepared, for example, using DNA with the nucleotide sequence

Page 18, please replace paragraph 5, with the following amended paragraph:

The present invention further provides antibodies with affinity to the calcium-binding protein. The present invention relates to, for example, antibodies with affinity to or produced against the calcium-binding protein with the amino acid sequence encoded by the nucleotide sequence listed as in SEQ ID NO: 1 or 12, and fragments of the antibody. The antibodies may be produced against either the native or the recombinant form of the calcium-binding protein.